TRANSLATION OF THE ANNEXES TO THE IPER

Process for the catalyst-free preparation of cyanophenols from methoxybenzonitriles

Description

The present invention provides a process for the catalyst-free preparation of cyanophenols.

A common, industrially established process for preparing phenols which is described in detail in the literature [K. Weissermel, H.-J. Arpe, Industrielle organische Chemie [Industrial organic chemistry], 3rd revised and extended edition, VCH Weinheim, 1988, p. 376] is the known conversion of an isopropylaromatic using oxygen and the subsequent conversion to the phenol and acetone (Hock phenol synthesis). Disadvantages of this process are the equimolar occurrence of acetone and the high consumption of propene to prepare the isopropylaromatic. In addition, it is not possible to prepare arbitrarily substituted cyanophenols by this process.

In the already classic process [K. Weissermel, H.-J. Arpe, Industrielle organische Chemie [Industrial organic chemistry], 3rd revised and extended edition, VCH Weinheim, 1988, p. 370] for preparing phenols from benzenesulfonic acids, large amounts of salts (Na_2SO_3, Na_2SO_4) are obtained as a coproduct, so that the process can no longer be used in the western world for environmental reasons.

The preparation of phenols from chloroaromatics by means of NaOH is also known from the literature and has been industrially realized [K. Weissermel, H.-J. Arpe, Industrielle organische Chemie [Industrial organic chemistry], 3rd revised and extended edition, VCH Weinheim, 1988, p. 372], but in particular the

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necessary, sometimes drastic reaction conditions and particularly the temperatures above 360°C are regarded as disadvantageous. A conversion of the process to substituted phenols, for example
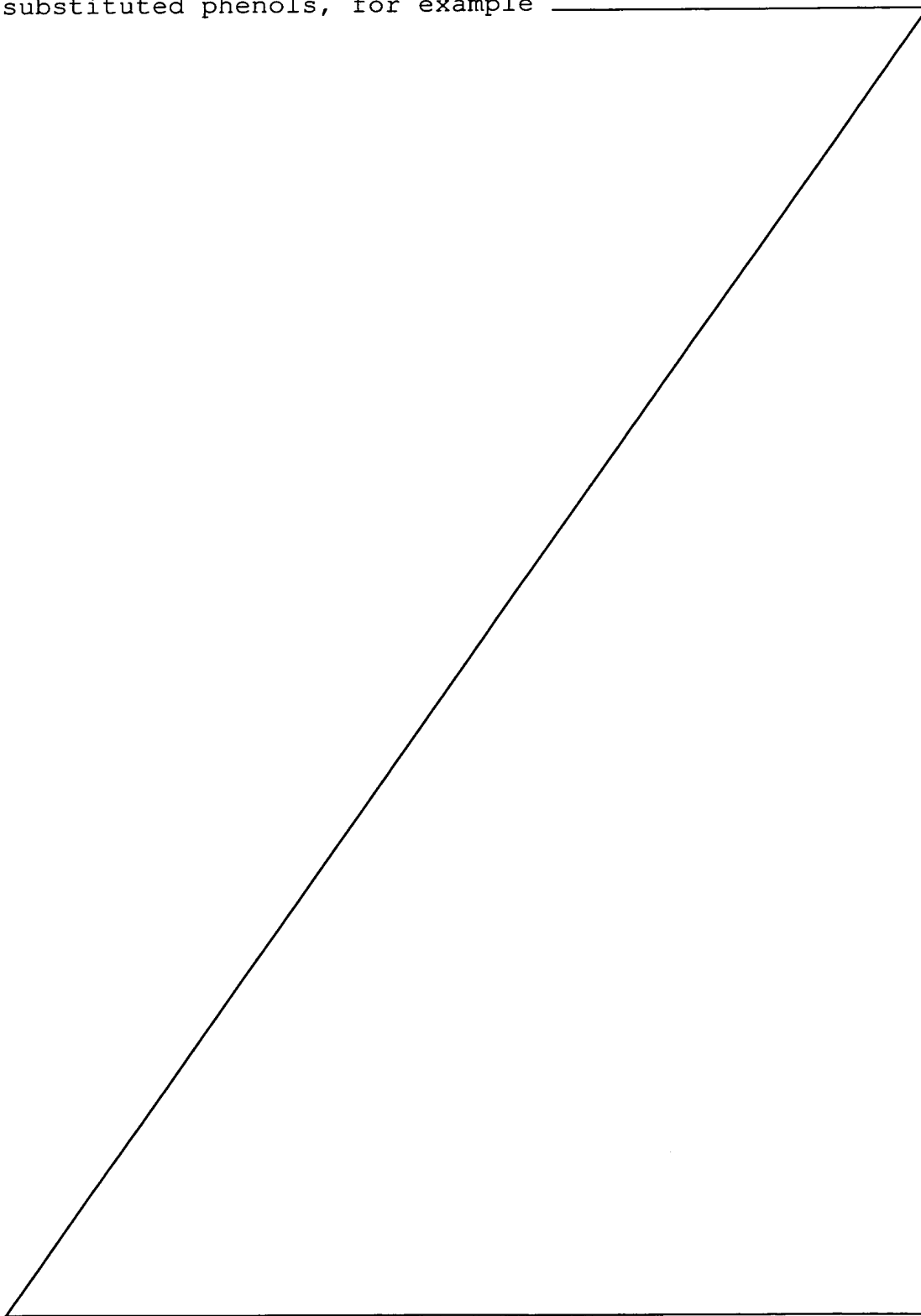
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Also known from the literature is the ammoxidation of methylphenols to the corresponding cyanophenols [M. V. Landau et al., Applied Catalysis A: General (2001), 208(1,2), 21-34; A. Martin et al., J. Prakt. Chem. (1990), 332(4), 551-6; H. Bruins Slot, DE 20 37 945], which succeeds, though, in only very modest yields. Disadvantages of this process are not only the low yield but also the high cost of inconvenience for the industrial synthesis. The same applies for the formation of the nitrile function from a benzoic acid and ammonia or from an ester and ammonia, according to the following references [R. Ueno et al., EP 74 116; M. Araki et al., JP 53040737; R. Perron, FR 2 332 261; G. Bakassian, M. Lefort, DE 22 05 360; H. Eilingsfeld, E. Schaffner, DE 20 20 866; T. Ichii et al., JP 43029944].

The literature also gives details on the ether cleavage to form phenols [P. R. Brooks et al., Journal of Organic Chemistry (1999), 64(26), 9719-9721]. In this process, especially the stoichiometric use of the expensive raw materials boron trichloride and the use of large amounts of n-butylammonium iodide are regarded as disadvantageous.

Systems which have been developed specifically for the cleavage of allyl ethers are also described in the present context. To this end, it is possible to use systems composed of $CeCl_3$ and NaI [R. M. Thomas et al., Tetrahedron Letters (1999), 40(40), 7293-7294] or $NaBH_4$ [R. M. Thomas et al., Tetrahedron Lett. (1997), 38(26), 4721-4724], or else electrochemical processes

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[D. Franco et al., Tetrahedron Lett. (1999), 40(31), 5685-5688; A. Yasuhara et al., J. Org. Chem. (1999), 64(11), 4211-4213; K. Fujimoto et al., Tetrahedron (1996), 52(11), 3889-96; S. Olivero et al., J. Chem. Soc., Chem. Commun. (1995), (24), 2497-8]. However, the latter process variant is expensive and it always requires the use of heavy metals; in addition, this process variant is restricted exclusively to the allyl ethers which are difficult to synthesize.

The preparation of nitrophenols from nitroaromatics by substituting hydrogen with hydroperoxide anions in the presence of strong bases is a very interesting process, but is unfortunately restricted to nitroaromatics; in addition, it is necessary to use liquid ammonia and readily decomposable and thus dangerous hydroperoxides [M. Makosza et al., J. Org. Chem. 1998, 63, 4199-4208]. To prepare cyanophenols, the nitro group has to be converted to a cyano group in a complicated manner.

T. Senba and K. Sakano (JP 09023893) and H. Semba et al. describe the enzymatic synthesis of phenols [Appl. Microbiol. Biotechnol. 1996, 46, 432-437]. However, the low space-time yields and the long reaction times mean that this process cannot be utilized in an economic manner.

The synthesis of phenols from anilines by diazotization and decomposition of the diazonium compound in the presence of metals, particularly copper salts, has also been known for some time. Even though more recent studies have attempted to optimize the process [B. C. Gilbert et al., EP 596 684], this route nevertheless always leads via a diazonium compound which is difficult to handle.

According to S. Prouilhac-Cros et al., the preparation of phenols from arylsilanes with H_2O_2 and stoichiometric

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amounts of fluoride leads to phenols in good yields [Bull. Soc. Chim. Fr. 1995, 132, 513-16]. However, the arylsilane required is not sufficiently available in industrial quantities.

The synthesis of phenols from aryl methyl ethers with ethanethiolates is restricted to laboratory applications [J. A. Dodge et al., J. Org. Chem. 1995, 60, 739-41]. For industrial syntheses, the reaction is unsuitable because toxic and malodorous sulfur compounds are obtained.

The cleavage of aryl methyl ethers with the FeO/glacial acetic acid/oxygen system has likewise been described [A. F. Duprat et al., J. Mol. Catal. 1992, 77]. This process is restricted to particularly activated aromatics and gives the desired products only in low to very low yields. Only slightly better yields in the cleavage of aryl methyl ethers are obtained with $AlCl_3$/NaCl [G. Adamska et al., Biul. Wojsk, Akad. Tech. 1980, 29, 93-99]. The large amounts of inorganic waste which form do not allow any industrial application of the process. The $AlCl_3$/Ni system which is described in the literature for the cleavage of these ethers also does not offer any advantages whatsoever, since temperatures above 240°C and long reaction times are required [H. Kashiwagi, S. Enomoto, Yakugaku Zasshi 1980, 100, 668-71].

A very complicated process for the cleavage of aryl methyl ethers and for the preparation of hydroxybenzo-nitrile is transmethylation (for example FR 1 565 812), in which the reaction of methoxybenzonitrile with the sodium salt of cresol to the sodium salt of hydroxy-benzonitrile and methoxycresol is effected at temperatures above 200°C. This process affords large amounts of waste and has a very complicated procedure. Although aryl methyl ethers in principle constitute

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very suitable raw materials, the cleavage of the ether
is very difficult; alternative cleavage processes are
not available.

5   US-A-3,567,758 describes a process for preparing
4-alkoxybenzonitriles, in which, however, alkoxides are
not used, but rather sodium 4-methylphenoxide (sodium
phenoxide).

10   Alkoxides have in fact already been used for the
synthesis of phenols (see, for example, Testaferri et
al., The Reaction of Unactivated Aryl Halides with
Sodium Methoxide in HMPA, Tetrahedron 39, 1, 193-197
(1983)). However, this publication does not address in
15   any depth the preparation of cyanophenols.

GB 1,065,936 from 1967 discloses a process for
preparing 4-hydroxybenzonitrile by reacting anisic acid
with a nitrile.
20
EP 0 421 385 discloses a process for preparing an
hydroxyneophyl m-phenoxybenzyl ether using a lower
alkoxide. Here too, however, there is no information on
the preparation of cyanophenols.
25
All processes mentioned lead to the desired products
and have also already been used successfully for a
large number of highly varying applications. However,
all of these processes for preparing phenols and
30   especially cyanophenol have the disadvantage that they
have a very complicated procedure, that expensive raw
materials have to be used, that large amounts of waste
are formed or that the yield is only very low.

35   It is therefore an object of the present invention to
develop a process for the catalyst-free preparation of
cyanophenols, which allows the environmentally friendly

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and low-waste preparation of the desired product with favorable raw materials in high yields. In particular, the use of heavy metals, as is customary, for example, when metals are used as the catalyst, should be

5   dispensed with.

This object is achieved by a corresponding process, in which a substituted methoxybenzonitrile of the general formula (I)

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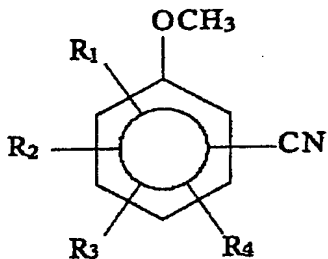
where

R$_1$, R$_2$, R$_3$ and R$_4$ are each independently hydrogen, a

15   C$_{1-10}$-alkyl, C$_{2-8}$-alkoxy, aryl, a

                                   phenoxy or a further nitrile group

is reacted with an alkali metal alkoxide at temperatures between 80 and 230°C.

20   It has been found, surprisingly, that not only is it possible, as desired, to dispense fully with catalysts for the performance of the reaction, and that the cyanophenols are obtained in very good yields and purities, but also that a relatively simple process

25   which can be performed without the occurrence of by-products on the industrial scale without any problems is thus available.

The selection of the aromatic raw materials is not

30   restricted only to simple methoxybenzonitriles, but rather also includes substituted methoxybenzonitriles, and in particular di-, tri-, tetra- or pentamethoxy-

benzonitriles are suitable.

Preferred alkali metal alkoxide components are methoxides and, among these, in particular sodium methoxide.

The process according to the invention can be carried out within a relatively large temperature range. However, particularly suitable reaction temperatures have been found to be between 120 and 200°C and most preferably between 140 and 180°C.

Typically, the reaction succeeds at best when the molar ratio of the methoxybenzonitrile component to the alkali metal alkoxide component is from 1:0.5 to 1.5 and more preferably 1:1.0 to 1.1.

Typically, the present process succeeds even without the presence of a solvent. However, the present invention also provides for the use of a suitable solvent, for which either polar or nonpolar solvents may be used. Particular preference is given to C_{1-6}-alcohols, for example methanol, and/or a solvent from the group of tetrahydrofuran, benzene, toluene, xylene and methyl tert-butyl ether. Especially suitable for practical reasons and for reasons of cost is the use of simple alcohols, for example methanol.

The preferred reaction is typically carried out by initially charging the alkoxide component in an alcohol (for example sodium methoxide in methanol), then adding the methoxybenzonitrile component, which is preferably effected with stirring; this should preferably be effected in an autoclave, in which case

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What is claimed is:

1. A process for the catalyst-free preparation of cyanophenols from methoxybenzonitriles, characterized in that a substituted methoxybenzonitrile of the general formula (I)
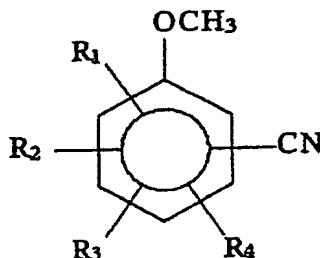
where
R$_1$, R$_2$, R$_3$ and R$_4$ are each independently hydrogen, a C$_{1-10}$-alkyl, C$_{2-8}$-alkoxy, aryl, a phenoxy or a further nitrile group
is reacted with an alkali metal alkoxide at temperatures between 80 and 230°C.

2. The process as claimed in claim 1, characterized in that the methoxybenzonitrile component used comprises di-, tri- tetra- or pentamethoxybenzonitriles.

3. The process as claimed in either of claims 1 and 2, characterized in that the alkali metal alkoxide used is a methoxide, more preferably sodium methoxide.

4. The process as claimed in one of claims 1 to 3, characterized in that it is carried out at temperatures between 120 and 200°C and more preferably between 140 and 180°C.

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5. The process as claimed in one of claims 1 to 4, characterized in that the molar ratio of the methoxybenzonitrile component to the alkali metal alkoxide component is 1:0.5 to 1.5 and more preferably 1:1.0 to 1.1.

6. The process as claimed in one of claims 1 to 5, characterized in that it is carried out in the presence of a polar and/or nonpolar solvent, more preferably in the presence of a C_{1-6}-alcohol, e.g. methanol, and/or of a solvent from the group of tetrahydrofuran, benzene, toluene, xylene and methyl tert-butyl ether.

7. The process as claimed in one of claims 1 to 6, characterized in that the alkoxide component is initially charged in an alcohol, then the methoxy-benzonitrile component is added and preferably heated with stirring, which is more preferably effected in an autoclave.

8. The process as claimed in one of claims 1 to 7, characterized in that the methoxybenzonitrile component has been prepared by ammoxidizing a methoxytoluene and in the presence of ammonia and (atmospheric) oxygen.

9. The process as claimed in claim 8, characterized in that the methoxybenzonitrile component is reacted further after the ammoxidation directly without isolation.

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